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FACSIMILE COVER SHEET

Date: August 1, 2008

To: **Examiner Layla D. Bland, Group Art Unit 1623** Fax No.: 571-273-9572
571-273-8300

Confirmation No. 6815

From: Warren M. Cheek

Number of pages being transmitted, including this cover sheet: 10

Please direct all questions concerning the transmittal of these pages to Donna King.

RE: Serial No. 10/578,359 (Shirou SAWA), filed June 6, 2006

MESSAGE:

Enclosed please find a Supplemental Reply along with an executed Declaration Under 37 CFR 1.132 of Mr. Sawa.

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	**Confirmation No. 6815**
Shirou SAWA	:	Attorney Docket No. 2006_0587A
Serial No. 10/578,359	:	Group Art Unit 1623
Filed June 6, 2006	:	Examiner Layla D. Bland
AQUEOUS SOLUTION PREPARATION CONTAINING AMINOGLYCOSIDE ANTIBIOTIC AND BROMFENAC	:	**Mail Stop: Amendment**

SUPPLEMENTAL REPLY

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Attached herewith is a Declaration by Mr. Sawa, the inventor of the present application. In the Declaration, Test-1 corresponds to Working Example 2 of the specification and Test-2 corresponds to Working Example 3 of the specification. The Declaration clearly shows that stable aqueous solutions without precipitation are obtained by adding monoethanolamine, N-methylglucamine or nicotinamide to an aqueous solution comprising an aminoglycoside antibiotic and Bromfemac. Applicants note Fu et al. (USP 5,414,011) fails to disclose or suggest that an aqueous solution preparation containing an aminoglycoside antibiotic, Bromfemac and monoethanolamine, N-methylglucamine or nicotinamide does not cause precipitation. Further, Cagle et al. (USP 6,440,964) fails to disclose or suggest the same.

Thus, in light of this Declaration, and in light of the arguments and claim amendments submitted May 21, 2008, the 35 USC 103 obviousness rejection over Fu et al. in view of Cagle et al. is untenable and should be withdrawn.

In view of the foregoing, it is believed that each ground of rejection set forth in the Office Action has been overcome, and that the application is now in condition for allowance.

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Accordingly, such allowance is solicited.

Respectfully submitted,

Shirou SAWA

By: _____
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CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that this paper is being facsimile transmitted to the Patent and Trademark Office on the date shown below.

Donna L. King
name of person signing certification

Signature

August 1, 2008
Date

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of
Serial No. 10/578,359
Shirou SAWA
Filed: June 6, 2006

Confirmation No. 6815
Group Art Unit: 1623
Examiner: Layla D. Bland

DECLARATION UNDER 37 CFR 1.132

Honorable Commissioner of Patents and Trademarks

Sir,

I, Shirou Sawa declare that:

I was born in Tokushima Prefecture, Japan, in 1965;

I am an inventor of the above-identified U.S. patent Application;

I am a citizen of Japan and a resident of Kobe-shi, Hyogo, Japan;

I graduated from Department of Chemical Engineering, Factory of Engineering, The University of Tokushima, Tokushima, Japan in 1988;

I received the Master degree on the study of the chemical engineering at The University of Tokushima, Tokushima, Japan, in 1990;

I have been an employee of SENJU PHARMACEUTICAL CO., LTD., Japan, since 1990 up to this time, and have been engaged in the research on formulation of eye drops.

The experiment set out below was conducted under my supervision.

Experiment

The effects of additives in an aqueous solution preparation comprising an aminoglycoside antibiotic and bromfenac

1. Test-1 of the change in formulation

1.1 Test Method

A combination solution comprising tobramycin and bromfenac sodium as shown in Table 1 was prepared (formulation 1). Boric acid and borax were added to and dissolved in a fixed amount of purified water, and to this solution were added tobramycin and bromfenac sodium, followed by dissolution. Separately, each additive was added to and dissolved in the prescribed amount of purified water to give an additive solution (shown in Table 2). The above combination solution and the additive solution were mixed in a ratio of 1:1, and the mixture was adjusted to a pH of 7.0 by addition of hydrochloric acid. The appearance of each sample solution was observed with the naked eye. The appearance was determined based on the following criteria.

Clear: the solution is transparent

Turbid: the solution is yellowish cloudy when viewed on a black background

Slightly turbid: the degree of the turbidity in the solution is lower compared to that of the above "turbid" criterion

Suspended: fine particles are floating in the solution,

and the solution is yellowish cloudy when viewed on a black background

Strongly turbid: fine particles are floating in the solution to such an extent that the background is not visible, or precipitates are formed.

Table 1

Formulation of combination solution	
	Formulation 1
Component	w/v%
Bromfenac sodium	0.2
Tobramycin	0.6
Boric acid	1.14
Borax	4.5
Hydrochloric acid	q.s.
Sodium hydroxide	q.s.
Purified water	q.s.

Table 2

Concentration of each additive in additive solutions	
Additive	w/v%
No additive (purified water)	0
Monoethanolamine	2.0
N-Methylglucamine	2.0
Nicotinamide	2.0

1.2 Test Results

The test results of the appearance of the combination solutions containing an additive were shown in Table 3.

Table 3

Additive	Final concentration	Appearance
Control (no additive)	-	turbid
Monoethanolamine	1.0 w/v%	clear
N-Methylglucamine	1.0 w/v%	slightly turbid
Nicotinamide	1.0 w/v%	clear

The above Table 3 indicates that the appearance is preferable in the order of "clear", "slightly turbid" and "turbid" for the aqueous solution preparations of the present invention. As apparent from Table 3, turbidity occurrence in the preparations was inhibited or reduced by adding an organic amine such as monoethanolamine and N-methylglucamine; or nicotinamide.

2. Test-2 of the change in formulation

2.1 Test Methods

Combination solutions comprising gentamicin sulfate and bromfenac sodium as shown in Table 4 were prepared (formulation 2). With respect to the formulation 2, boric acid and borax was added to and dissolved in a fixed amount of purified water, and to this solution were added gentamicin sulfate and bromfenac sodium, and then the mixture was dissolved. Separately, each additive solution was prepared as shown in Table 5. Each additive was added to and dissolved in a prescribed amount of water. The above combination solution and the additive solution were mixed in a ratio of 1:1. The resulting solutions were each adjusted to a pH of 6.5 by the addition of hydrochloric acid. The appearances of the mixed solutions thus prepared were

observed with the naked eye. The appearance was determined according to the criteria as described in Test 1.

Table 4

Component	Formulation of combination solution (w/v%)
	Formulation 2
Bromfenac sodium	0.2
Gentamicin sulfate	0.6
Boric acid	1.14
Borax	4.5
Hydrochloric acid	q.s.
Sodium hydroxide	q.s.
Purified water	q.s.

Table 5

Concentration of each additive in additive solutions	
Additive	w/v%
No additive (Purified water)	0
Monoethanolamine	2.0
N-Methylglucamine	2.0
Nicotinamide	2.0

2.2 Test results

The appearance of the solutions in the Test of the change in formulations was shown in Table 6 in terms of additives.

Table 6

Additive		Combination formulation	pH	Appearance
Component	Final concentration (w/v%)			
Control (No additive)	-	Formulation 2	6.5	Suspended
Monoethanolamine	1.0	Formulation 2	6.5	clear
N-Methylglucamine	1.0	Formulation 2	6.5	Slightly turbid
Nicotinamide	1.0	Formulation 2	6.5	Clear

In the above Table 6, the appearances of the solutions are preferable in the order of "clear", "slightly turbid", and "turbid" for the aqueous solution preparation of the present invention. The preparation with "suspended" is not preferred for the aqueous solution preparation of the present invention. As clearly seen from Table 6, turbidity occurrence in the preparations are inhibited or reduced by adding an organic amine such as monoethanolamine and N-methylglucamine; or nicotinamide.

3. Conclution

It is clear from the above Test results that a stable aqueous solution wherein no precipitation occurred was provided by adding monoethanolamine, N-methylglucamine or nicotinamide to the aqueous solution comprising an aminoglycoside antibiotic and Bromfenac.

It is declared by the undersigned that all statements made herein of undersigned's own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001, and that such willful false statements may jeopardize the validity of the above-identified application or any patent issuing thereon.

This 22 day of July, 2008

Shirou Sawa

Shirou Sawa,